



Institute for In Vitro Sciences, Inc.



ICCVAM Eye Tests Comments to the Expert Panel

Presented By
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Validation of Methods

- International agreement that new safety tests should generally provide an equivalent level of protection as existing tests.
- This brings up the important question: How do we determine if the new test provides the level of protection provided by the current test?
- One estimate - “How well does the current test predict the human response?” - can’t be done here.
- Second estimate – “How often does a new method classify a test material the same way as the animal test?” One way to set a standard is to ask how well the existing test does the same task.

Before you can begin to consider validation, you must (as far as possible) understand the performance of the animal test!

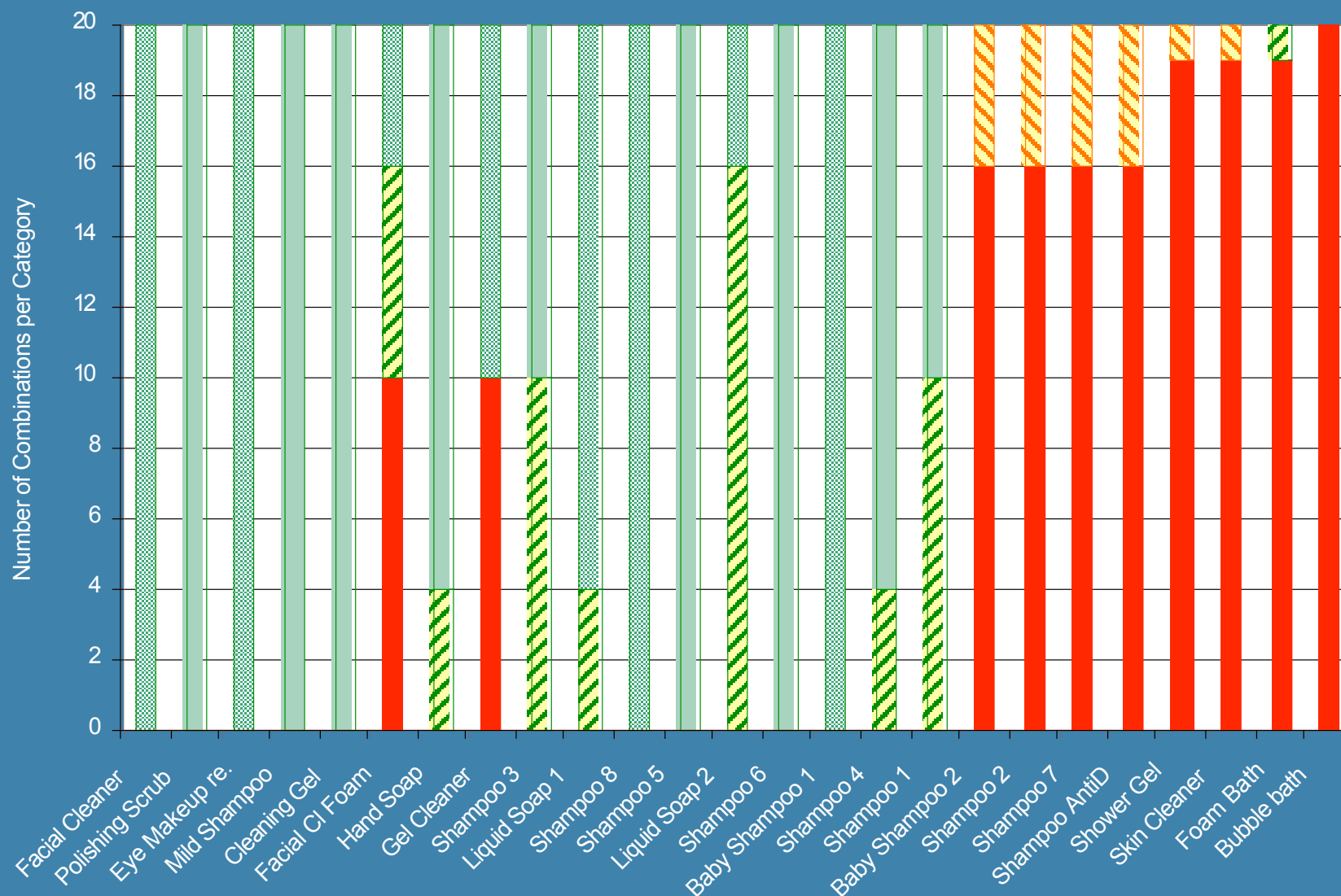
What do the Statistics Mean in Practice?

- CTFA Evaluation (1993-1994) used randomized block design for animal testing to estimate variability
- Still not representative of between-laboratories variability – in real life variability will likely be worse!
- All originally 6 rabbit tests, so results (categories) of all possible sets of three rabbits can be calculated
- **Results are that you may categorize the test substances differently each time you run the test.**
- Therefore an in vitro test should have to perform no better than that.

CTFA Phase III Data

Name	Material	GHS Category		GHS 2b	GHS NI	% Under	# uncleared
		GHS 1	GHS 2a				
Shampoo 5	HZD*				20	na	0
Shampoo 8	HZG*				20	na	0
Eye Makeup re.	HZH				20	na	0
Mild Shampoo	HZJ				20	na	0
Shampoo 3	HZM*				20	na	0
Shampoo 6	HZN*				20	na	0
Baby Shampoo 1	HZP				20	na	0
Cleaning Gel	HZQ				20	na	0
Polishing Scrub	HZT				20	na	0
Facial Cleaner	HZZ				20	na	0
Liquid Soap 1	HZB*			4	16	na	0
Hand Soap	HZU*			4	16	na	0
Shampoo 4	HZV*			4	16	na	0
Shampoo 1	HZC*			10	10	na	0
Liquid Soap 2	HZW*			16	4	na	0
Gel Cleaner	HZE	10		0	10	50%	1
Facial CI Foam	HZR*	10		6	4	50%	1
Shampoo 7	HZA	16	4			20%	2
Baby Shampoo 2	HZF	16	4			20%	2
Shampoo 2	HZX	16	4			20%	2
Shampoo AntiD	HZY	16	4			20%	2
Skin Cleaner	HZI	19	1			5%	3
Shower Gel	HZS	19	1			5%	3
Foam Bath	HZL	19		1		5%	3
Bubble bath	HZK	20				0%	5

CTFA Phase III Data – GHS Categories

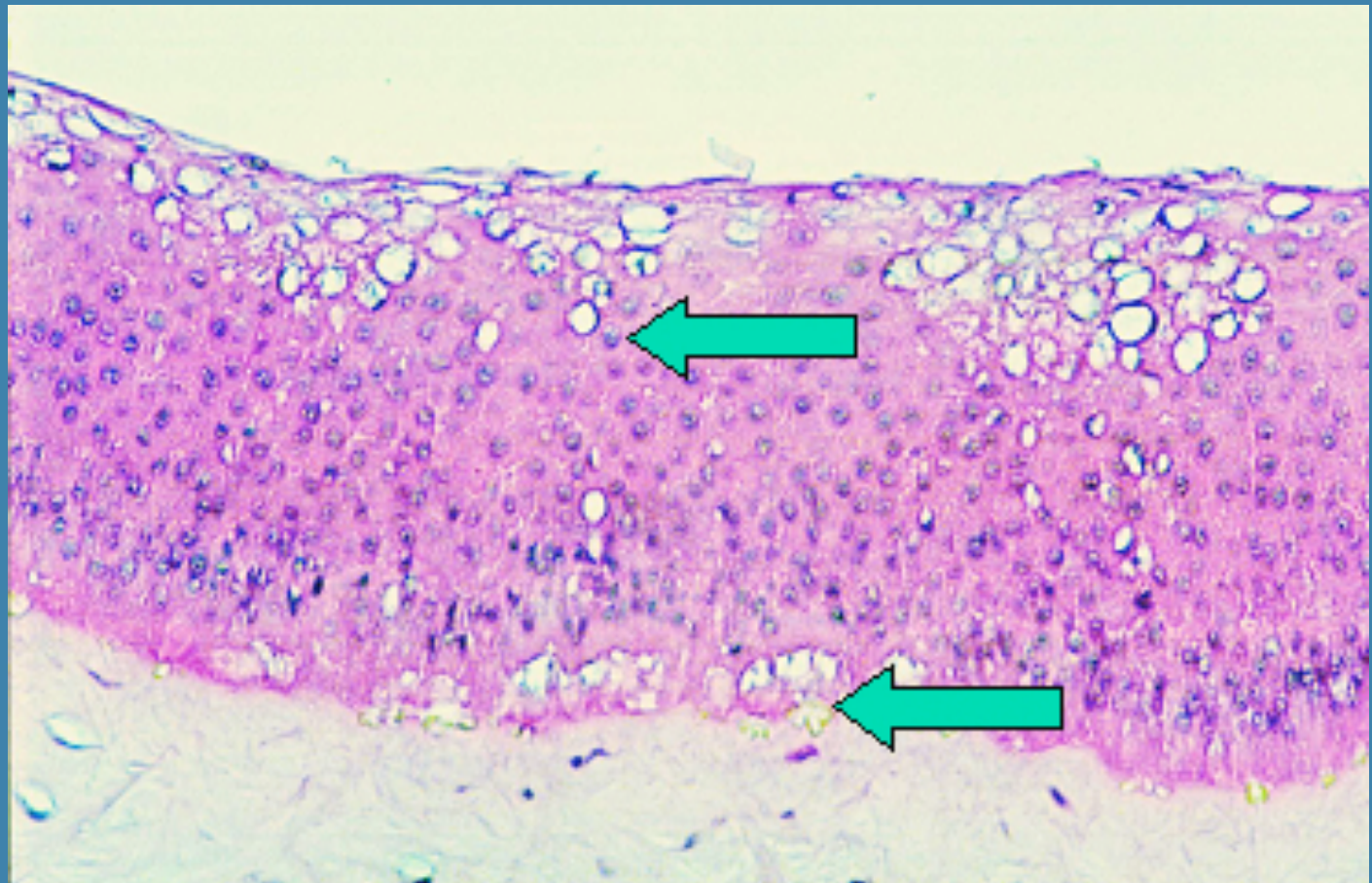


How Can We Really Tell if a Test is “Good Enough”?

- Examine its relevance
 - Does it have a reasonable biological relationship to the tissue(s) to be modeled?
 - Is it capable of responding to the same modes of action that are known to be part of the toxic response in vivo?
 - Is it possibly more closely related to the human than it is to the animal model?
 - What are its relevant performance statistics?

Histology of EC/HO Materials

Sodium
Oxalate



Quinacrine



